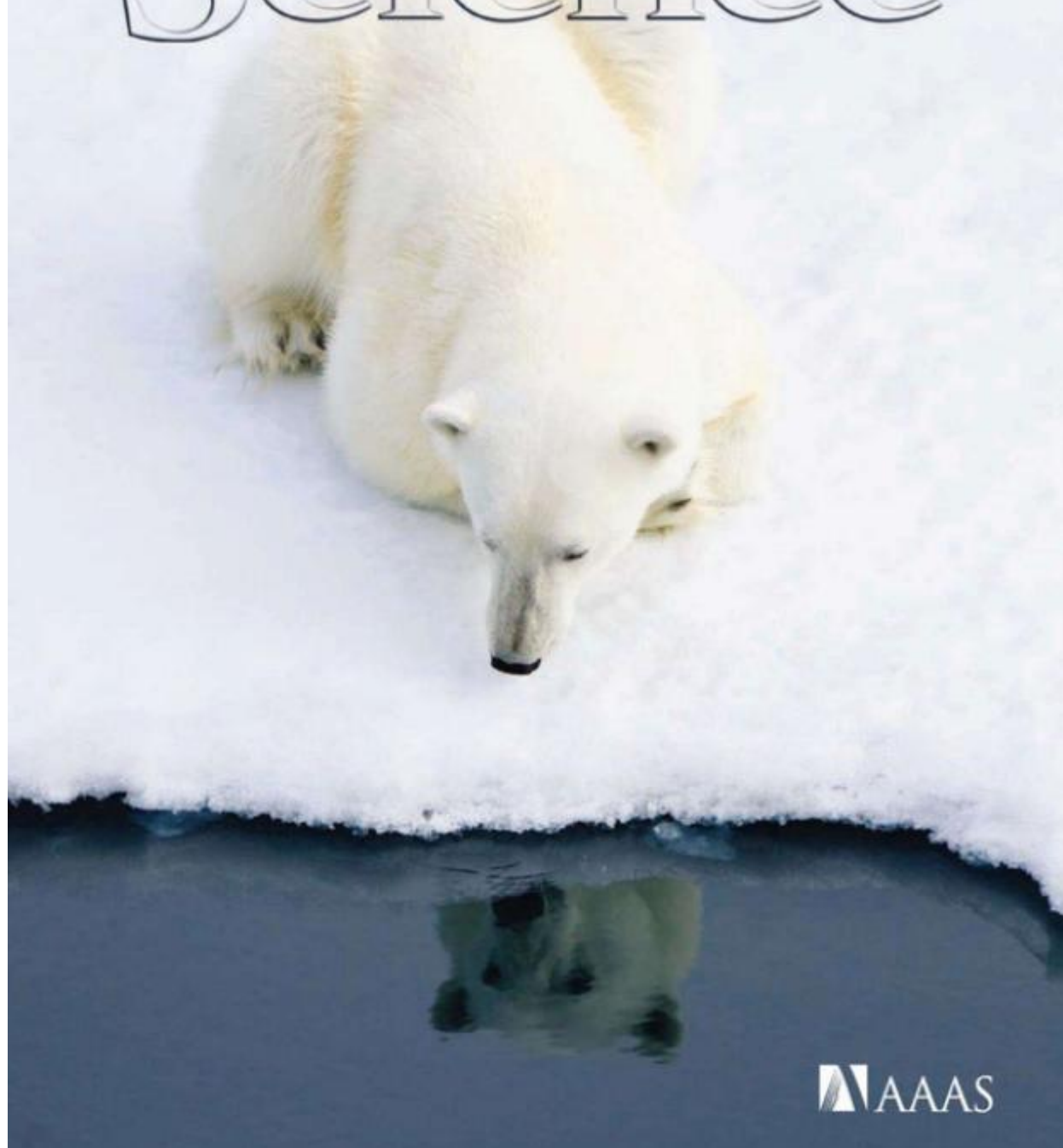


Science

20 April 2012 | \$10



AAAS

EDITORIAL

- 276 Standards for Postdoc Training
Alan I. Leshner

NEWS OF THE WEEK

- 280 A roundup of the week's top stories

NEWS & ANALYSIS

- 283 Dread Citrus Disease Turns Up in California, Texas
>> Science Podcast
- 284 Texas Medical Board Approves Rules for Controversial Treatments
- 285 Will Dutch Allow 'Export' of Controversial Flu Study?
>> See all HSNL coverage online at <http://sciencemag.org/hsnl>
- 286 Nanoparticle Treatment Reverses Cerebral Palsy in Rabbits
>> Science Translational Medicine Research Article by S. Kannan et al. and Focus by S. Ito; News story p. 292
- 287 Saving Money Essential for Next Census, Says Departing Director

NEWS FOCUS

- 288 Trouble on the Yangtze
Evidence Mounts for Dam-Quake Link
- 292 American Chemical Society Spring Meeting
Nanoparticles Offer 'Open Sesame' Keys to New Drugs and Vaccines
Biofuels and City Air: A Marginal Effect
New Genetic Letters Augment DNA, and Soon Perhaps Life
>> News story p. 286; Report p. 341

LETTERS

- 295 Environment-Friendly Reform in Myanmar
E. L. Webb et al.
- India's Science: Elitism Prevails
S. P. Bhat
- India's Science: Excellence Unrecognized
T. Abbasi and S. A. Abbasi
- 296 CORRECTIONS AND CLARIFICATIONS
- 296 TECHNICAL COMMENT ABSTRACTS
- BOOKS ET AL.
- 297 Am I My Genes?
R. L. Kitzman, reviewed by M. A. Goldman
- 298 Environmental Literacy in Science and Society
R. W. Scholz et al., reviewed by H. A. Mieg

POLICY FORUM

- 299 FDA's Approach to Regulation of Products of Nanotechnology
M. A. Hamburg

PERSPECTIVES

- 301 A Dive to Challenger Deep
R. A. Lutz and P. G. Falkowski
- 302 Solution-Processible Electrodes
M. G. Helander
>> Report p. 327
- 303 Tapping into the Wisdom of the Crowd—With Confidence
R. Herwig
>> Report p. 360
- 304 Heterogeneity and Tumor History
D. Shibata
- 306 Making Waves for Segments
S. Roth and K. A. Parfitt
>> Report p. 338
- 307 Toward an Alternative Biology
G. F. Joyce
>> Report p. 341
- 308 Visualizing Amyloid Assembly
D. Elizer
>> Report p. 362

CONTENTS continued >>



page 288



page 297



COVER

A young polar bear (*Ursus maritimus*) on a piece of ice that is drifting in the Barents Sea, northeast of Svalbard, Norway. Polar bears depend on sea ice as a platform for hunting seals, but current melting and retreat of sea ice is increasingly forcing them onto land. A recent study has found polar bears to be evolutionarily older and genetically more distinct than was previously thought. See page 344.

Photo: Florian Schulz, www.visionsofthewild.com

DEPARTMENTS

- 274 This Week in Science
- 277 Editors' Choice
- 278 Science Staff
- 367 New Products
- 368 Science Careers



page 301



page 310



pages 348 & 351

REVIEW

- 310 The State and Fate of Himalayan Glaciers
T. Bolch et al.

RESEARCH ARTICLE

- 315 Oxidation of the Guanine Nucleotide Pool Underlies Cell Death by Bactericidal Antibiotics
J. J. Fari et al.
Several antibiotics kill bacteria by causing oxidative damage to guanine nucleotides, which then damage nucleic acids.

REPORTS

- 320 Interplay of Intra- and Intermolecular H-Bonding in a Progressively Solvated Macrocyclic Peptide
N. S. Nagorova et al.
The main conformational changes associated with the hydration of a peptide ring arise upon the addition of just two water molecules.
- 324 Enantioselective C-H Croylation of Primary Alcohols via Hydroxyalkylation of Butadiene
J. R. Ziegler et al.
A catalyst facilitates complex carbon-carbon bond formation using a bulk commodity feedstock compound.
- 327 A Universal Method to Produce Low-Work Function Electrodes for Organic Electronics
Y. Zhou et al.
Air-stable, physisorbed polymers containing aliphatic amine groups can improve the efficiency of organic electronic devices.
»» Perspective p. 302
- 332 Dislocation Damping and Anisotropic Seismic Wave Attenuation in Earth's Upper Mantle
R. J. M. Farla et al.
Stress built up from plate tectonic collisions dissipates at dislocations in mantle minerals.
- 335 Dynamic Causes of the Relation Between Area and Age of the Ocean Floor
N. Calice et al.
Numerical simulations show that the presence of continents influences the area of old sea floor.
- 338 A Segmentation Clock with Two-Segment Periodicity in Insects
A. E. Samarin et al.
Oscillating gene expression, a key feature of vertebrate segmentation, is shown to occur during segmentation in beetles.
»» Perspective p. 306

- 341 Synthetic Genetic Polymers Capable of Heredity and Evolution
V. B. Pinheiro et al.
Artificial polymers of nucleic acid-like subunits not found in nature can mimic the functions of DNA and RNA.
»» News story p. 292; Perspective p. 307; Science Podcast
- 344 Nuclear Genomic Sequences Reveal that Polar Bears Are an Old and Distinct Bear Lineage
E. Hailer et al.
Genomic analyses show that polar bears as a species are older and genetically more distinct than previously estimated.
- 348 A Common Pesticide Decreases Foraging Success and Survival in Honey Bees
M. Henry et al.
Honey bees cannot find their way home after exposure to sublethal doses of a widely used insecticide.
- 351 Neonicotinoid Pesticide Reduces Bumble Bee Colony Growth and Queen Production
P. R. Whitthorn et al.
Bumble bee colonies produce many fewer queens after exposure to a widely used insecticide.
- 353 Recent Plant Diversity Changes on Europe's Mountain Summits
H. Paul et al.
European mountaintop flower species richness is increasing on northern summits but decreasing on southern summits.
- 355 A Yeast Prion, Mod5, Promotes Acquired Drug Resistance and Cell Survival Under Environmental Stress
G. Suzuki et al.
Conversion of a soluble prion protein to an aggregated state generates heritable resistance to antifungal drugs.
- 360 When Are Two Heads Better than One and Why?
A. Kioria
Group decisions may reflect the confidence of individual choices rather than accuracy.
»» Perspective p. 303; Science Podcast
- 362 Structure of an Intermediate State in Protein Folding and Aggregation
P. Neudecker et al.
A folding intermediate of a protein SH3 domain is prone to aggregation, which competes with native folding.
»» Perspective p. 308

SCIENCEONLINE

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The Ancient Drug Salicylate Directly Activates AMP-Activated Protein Kinase

S. A. Hawley et al.

A possible molecular mechanism of action for a metabolite of aspirin is described.

10.1126/science.1215327

Don't Look Back in Anger! Responsiveness to Missed Chances in Successful and Unsuccessful Aging

S. Bransen et al.

Emotionally healthy older adults show a reduced responsiveness to regret when performing a sequential decision task.

10.1126/science.1217516

Strongly Interacting Rydberg Excitations of a Cold Atomic Gas

Y. O. Dudin and A. Kuzmich

Illumination of an ensemble of cold rubidium atoms ultimately leads to high-level excitation of just a single atom.

10.1126/science.1217901

The Active Site of Methanol Synthesis over CuZnO/Al₂O₃ Industrial Catalysts

M. Behrens et al.

Catalysis is favored by stepped copper nanoparticles decorated with zinc oxide, which promotes stronger intermediate binding.

10.1126/science.1219831

TECHNICAL COMMENTS

Comment on "Detection of Emerging Sunspot Regions in the Solar Interior"

D. C. Braun

Full text at: www.sciencemag.org/cgi/content/full/336/6079/296-c

Response to Comment on "Detection of Emerging Sunspot Regions in the Solar Interior"

S. J. Moros et al.

Full text at: www.sciencemag.org/cgi/content/full/336/6079/296-d

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http://scim.ag/Facial_Expressions

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E. Arin

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D. Jensen

Scientists and other professionals can increase their job satisfaction by kicking their addiction to praise.

http://scim.ag/PraiseAddiction

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The Signal Transduction Knowledge Environment

17 April Issue: http://scim.ag/sd041712

EDITORIAL GUIDE: Focus Issue—Adding Math to the Signaling Toolkit

W. Wong and J. F. Foley

Computational approaches can reveal how cells interpret, process, and respond to signals.

RESEARCH ARTICLE: Synthetic Signal Propagation Through Direct Cell-Cell Interaction

M. Matsuda et al.

PERSPECTIVE: Understanding Signaling Dynamics Through Synthesis

A. L. Sussarangkarn and R. Weiss

An engineered system based on Notch and Delta in mammalian cultured cells recapitulates signal propagation, a phenomenon that occurs in development.

RESEARCH ARTICLE: Quantifying Crosstalk Among Interferon- γ , Interleukin-12, and Tumor Necrosis Factor Signaling Pathways Within a T_H1 Cell Model

D. J. Ninkovic et al.

Combining experiments with mathematical modeling provides insights into the responses of T cells to cytokines.

PERSPECTIVE: Unmasking Functional Motifs Within Disordered Regions of Proteins

R. K. Das et al.

The application of a computational approach to identify short linear motifs may enable the engineering of signaling networks.

REVIEW: Computational Approaches for Analyzing Information Flow in Biological Networks

B. Kholodenko et al.

Signaling network construction and analysis provide insights into biology and medicine.

PROTOCOL: A Systematic Approach for Analysis of Peptide Array Kinome Data

Y. Li et al.

A new method of analysis of kinome data takes account of the differences between peptide arrays and DNA microarrays.

ST NETWATCH: Plant Metabolic Network (PMN)

An integrated network of researchers and data provide plant metabolic pathway models.

ST NETWATCH: Systems Biology Experiment Analysis Management System (SBEAMS)

Integrate microarray and proteomics data with a database manager and analysis package.

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18 April Issue: http://scim.ag/stm041812

FOCUS: The Power of One

D. Louvard et al.

A single mouse Lgr5-positive colon stem cell can be expanded into a 3D organoid that, after transplant, contributes to the repair of injured colon epithelia in a mouse model of colitis.

RESEARCH ARTICLE: Dendrimer-Based Postnatal Therapy for Neuroinflammation and Cerebral Palsy in a Rabbit Model

S. Kannan et al.

FOCUS: A Baby Step for Nano

S. Ito

A dendrimer-drug conjugate attenuates neuroinflammation and improves motor function in a rabbit model of cerebral palsy.

>> News story p. 286

RESEARCH ARTICLE: Patient-Specific Induced Pluripotent Stem Cells as a Model for Familial Dilated Cardiomyopathy

N. Sun et al.

Cardiomyocytes derived from iPSC cells from patients with familial dilated cardiomyopathy can be used to model this disease.

RESEARCH ARTICLE: Targeted Delivery of PLK1-siRNA by ScFv Suppresses Her2+ Breast Cancer Growth and Metastasis

Y. Yao et al.

Antibody-mediated delivery of anticancer small interfering RNAs suppresses Her2+ breast cancer growth and metastasis.

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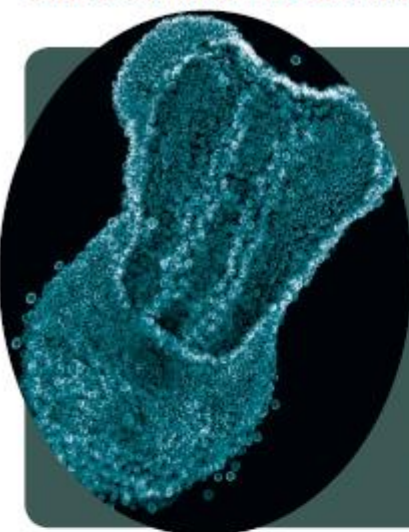
On the 20 April Science Podcast: synthetic genetics, confidence in decision-making, California's citrus crisis, and more.

SCIENCE (ISSN 0036-8073) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Intellectual Mail postage (publication No. 494-040) paid at Washington, DC, and additional mailing offices. Copyright © 2012 by the American Association for the Advancement of Science. The AAAS/SCM is a registered trademark of the AAAS. Domestic individual membership and subscription (US, Canada, Mexico, Caribbean, and Central America) \$125 (US\$135 for those in subscription). Domestic institutional subscription (US, Canada, Mexico, Caribbean, and Central America) \$1500 (US\$1600 for those in subscription). Foreign postage extra: Mexico, Caribbean (surface mail) \$15; other countries (air and surface) \$65. First class, airmail, surface, and member rates on request. Canadian rates with GST available upon request. GST #R123456789. Publication Mail Agreement Number 806424. Printed in the USA.

Change of address: Allow 4 weeks. Send change of address to AAAS, P.O. Box 940719, Washington, DC 20090-0719. Single-copy sales: \$5.00 (US\$5.50 back issue prepaid). Include surface postage. Bulk rates on request. Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that \$5.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for Science is 0036-8073. Science is indexed/abstracted in the following journals and is covered by several specialized indexes.



ADVANCING SCIENCE. SERVING SOCIETY



<< Tic-Toc Segmentation Clock

Molecular oscillators are an essential component of vertebrate segmentation, but whether they exist in segmented animals in general has been controversial for almost a decade. *Sarrasin et al.* (p. 338, published online 8 March; see the Perspective by Roth and Panfilio) demonstrate the existence of a segmentation clock in the growth zone of insects. Microsurgical manipulation and embryo culture revealed cyclic expression of the segmentation gene *Tc-odd* in the beetle *Tribolium castaneum*, which suggests that segmentation clocks are a widely shared mechanism that mediates animal segmentation.

Going More Slowly

Himalayan glaciers sometimes are called the "Third Pole" because of the amount of snow and ice they contain. Despite their importance as a global water reservoir and their essential role in Asian hydrology, how their mass is changing in response to global warming is not well known. *Bolch et al.* (p. 310) review the contemporary evolution of glaciers in the Himalayan region, including those of the less well sampled region of the Karakoram to the Northwest, in order to provide a current, comprehensive picture of how they are changing. Most Himalayan glaciers are retreating at rates comparable to glaciers elsewhere in the world. In the Karakoram, on the other hand, advancing glaciers are more common.

Unnatural Bases

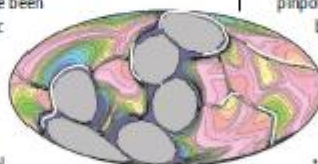
The genetic basis of all life on the planet is comprised of deoxyribonucleic acid (DNA) with four nitrogenous nucleotide bases, abbreviated to A, G, C, and T. But there are variations on this theme, and *Pinheiro et al.* (p. 341; see the Perspective by Joyce) describe the directed evolution of unnatural nucleic acid-like genetic polymers. Variant enzymes were developed that efficiently transcribed DNA to anhydronucleotides (HNA), cyclohexenyl (CeNA), locked (LNA), and thiofuranosyl (fNA) nucleic acid analogs. Further variant enzymes were developed to reverse-transcribe these analogs back to DNA. Thus, man-made nucleic acid analogs can be designed and selected that have the potential

to operate in a way analogous to the natural process of heredity and evolution.

Old Plates and the Sea

Estimates for the area and age of the ocean floor are at odds with assumptions for mantle convection, which imply that an older sea floor—rather than a new one—would be preferentially subducted over time. Previous efforts to explain these relationships have been

based on geologic evidence and simple models. *Coltice et al.* (p. 335) created numerical three-dimensional convection models representing more realistic physical boundaries, including a spherical Earth, the existence of continents and supercontinents over time, and realistic rheologies. A combination of continents and plate-like behavior of the ocean floor sufficed to produce the observed relationship between plate area and plate age, which explains why some old oceanic crust still remains.



A Specific Oxidative Catastrophe

Three different classes of antibiotics induce bacterial cell death by the production of hydroxyl radicals. Hydroxyl radicals are powerful oxidizing agents in living cells and will oxidize

the nucleic acid base, guanine, to form 8-oxoguanine, which is potentially mutagenic because it can pair with both cytosine and adenine and form lethal double-strand DNA breaks. *Foti et al.* (p. 315) discovered that overproduction of the nucleotide sanitizer Mufi, which hydrolyzes 8-oxo-dGTP to 8-oxo-dGMP, gives striking protection against cell death.

Bonded at the Source

Asymmetric catalysis is a relatively mature field in the laboratory, with a diverse array of techniques available for the selective transformation of organic compounds. However, scaling up these techniques for industrial application remains challenging, in part because many catalysts act best on reagents that have been expensively modified, although this process often generates copious waste. *Zbieg et al.* (p. 324, published online 22 March) combat this challenge with a ruthenium-based catalyst that couples an unmodified bulk commodity feedstock (butadiene) with alcohols, forming carbon-carbon bonds to generate complex products with high selectivity.

Hydrated in a Hurry

Water has a major influence on the conformation of proteins and related biomolecules. However, so many water molecules participate in the hydrogen bonding networks that it can be difficult to pinpoint which specific interactions play the biggest role. *Nagornova et al.* (p. 320) sought to answer this question for the case of a 10-amino acid ring—the antibiotic compound Gramicidin S—by probing the conformational impact of successive additions of one to 50 water molecules to the naked gas-phase structure. The primary changes in the overall ring geometry came from the addition of just the first two waters.

A Sturdy Electrode Coating

To operate efficiently, organic devices—such as light-emitting diodes—require electrodes that emit or take up electrons at low applied voltages (that is, have low work functions). Often these electrodes are metals, such as calcium, that are not stable in air or water vapor and have to be protected from environmental damage. *Zhou et al.* (p. 327; see the Perspective by Helander) report that a coating polymer containing aliphatic amine groups can lower the work functions of various types of electrodes by up to 1.7 electron volts and can be used in a variety of devices.

S